

We claim:

- 1 1. A method for determining steroid responsiveness in a subject, the method  
2 comprising the steps of:
- 3 (a) obtaining a tissue, body fluid or cell sample from a subject undergoing steroid  
4 treatment;
- 5 (b) determining a first level of expression of RNA from a first gene known or  
6 suspected to be steroid responsive;
- 7 (c) determining a second level of expression of RNA from a second gene known  
8 or suspected to be non-responsive to steroids; and
- 9 (d) comparing the first and second levels of RNA to create a ratio, wherein the  
10 subject is steroid responsive if the ratio is higher than a predetermined control ratio  
11 for untreated or nonresponsive subjects, or similar to prior ratios for the subject when  
12 the subject was previously determined to be responsive.

- 1 2. A method for determining steroid responsiveness in a tissue, body fluid or cell,  
2 the method comprising the steps of:
- 3 (a) exposing a tissue, body fluid or cell sample *in vitro* to a steroid;
- 4 (b) determining a first level of expression of RNA from a first gene known or  
5 suspected to be steroid responsive;
- 6 (c) determining a second level of expression of RNA from a second gene known  
7 or suspected to be non-responsive to steroids; and
- 8 (d) comparing the first and second levels of RNA to create a ratio, wherein the  
9 tissue, body fluid or cell sample is steroid responsive if the ratio is higher than a  
10 predetermined control ratio for untreated or nonresponsive subjects, or similar to prior  
11 ratios for the subject when the subject was previously determined to be responsive.

1 3. A method for determining steroid responsiveness in a subject, the method  
2 comprising the steps of:

3 (a) obtaining a pre-treatment tissue, body fluid or cell from a subject;

4 (b) determining a level of RNA expressed in the pre-treatment tissue, body fluid  
5 or cell from a first gene known or suspected to be responsive to steroids;

6 (c) determining a level of RNA expressed in the pre-treatment tissue, body fluid  
7 or cell from a second gene known or suspected to be un-responsive to steroids;

8 (d) administering a steroid to the subject;

9 (e) obtaining a post-treatment tissue, body fluid or cell from the subject after  
10 steroid administration;

11 (f) determining a post-treatment level of RNA expressed from the first gene;

12 (g) determining a post-treatment level of RNA expressed from the second gene;

13 (h) comparing the pre-treatment level of RNA expressed from the first gene to the  
14 pre-treatment level of RNA expressed from the second gene to create a first  
15 normalized value;

16 (i) comparing the post-treatment level of RNA expressed from the first gene to the  
17 post-treatment level of RNA expressed from the second gene to create a second  
18 normalized value;

19 (j) comparing the first normalized value to the second normalized value, wherein  
20 if the first normalized value is less than the second normalized value, it is indicative  
21 of steroid responsiveness in the tissue, body fluid or cell, and/or if the first normalized  
22 value is greater than or the same as the second normalized value, it is indicative of  
23 steroid non-responsiveness in the cell, and/or wherein the difference between the first  
24 normalized value and the second normalized value correlates to the ability of the  
25 subject to respond to the steroid.

1 4. A method for determining an effective dose of a steroid in a subject, the method  
2 comprising the steps of:

3 (a) administering to a subject a dose of a steroid;

4 (b) obtaining a tissue, body fluid or cell from the subject;

5 (c) determining a first level of expression of RNA from a first gene known or  
6 suspected to be steroid responsive;

7 (d) determining a second level of expression of RNA from a second gene known  
8 or suspected to be non-responsive to steroids; and

9 (e) comparing the first and second levels of RNA, wherein the difference between  
10 the first RNA level and the second RNA level is indicative of the effectiveness of the  
11 steroid dose in the subject.

1 5. A method for monitoring a subject's ability to respond to a steroid, the method  
2 comprising the steps of:

3 (a) administering to a subject a dose of steroid;

4 (b) obtaining a tissue, body fluid or cell from the subject;

5 (c) determining a first level of expression of RNA from a first gene known or  
6 suspected to be steroid responsive;

7 (d) determining a second level of expression of RNA from a second gene known  
8 or suspected to be non-responsive to steroids; and

9 (e) comparing the first and second levels of RNA to create a ratio, wherein the  
10 subject is steroid responsive if the ratio is higher than a predetermined control ratio  
11 for untreated or nonresponsive subjects, or similar to prior ratios for the subject when  
12 the subject was previously determined to be responsive.

6. A method for determining drug responsiveness in a subject undergoing drug treatment, the method comprising the steps of:

(a) obtaining a tissue, body fluid or cell from a subject undergoing treatment with a drug;

(b) determining a first level of expression of RNA from a first gene known or suspected to be drug-responsive;

(c) determining a second level of expression of RNA from a second gene known or suspected to be non-responsive to the drug; and

(d) comparing the first and second levels of RNA, wherein the subject is drug-responsive if the first level is higher than the second level and the subject is non-responsive to drug if the second level is higher than the first level.

7. A method for determining drug responsiveness in a tissue, body fluid or cell, the method comprising the steps of:

(a) obtaining a tissue, body fluid or cell;

(b) exposing the tissue, body fluid or cell *in vitro* to a drug;

(c) determining a first level of expression of RNA from a first gene known or suspected to be drug-responsive;

(d) determining a second level of expression of RNA from a second gene known or suspected to be non-responsive to the drug; and

(e) comparing the first and second levels of RNA, wherein the tissue, body fluid or cell is drug-responsive if the first level is higher than the second level and the tissue, body fluid or cell is non-responsive to the drug if the second level is higher than the first level.

- 1 8. The method of claim 1, wherein one or more of the determining steps requires  
2 amplification of the RNAs.
- 1 9. The method of claim 8, wherein one or more of the determining steps requires  
2 polymerase chain reaction (PCR) of the RNAs.
- 1 10. The method of claim 1, wherein one or more of the determining steps requires *in*  
2 *situ* detection of the first and second RNA.
- 1 11. The method of claim 1, wherein one or more of the determining steps requires  
2 direct probing of the RNA.
- 1 12. The method of claim 1, further comprising monitoring or tracking the steroid  
2 responsiveness over time to detect a change in responsiveness.
- 1 13. The method of claim 1, further comprising the step of administering one or more  
2 pro-inflammatory and/or anti-inflammatory mediators to the tissue, body fluid or cell.
- 1 14. The method of claim 13, wherein the pro-inflammatory mediator is selected from  
2 the group consisting of interleukin 1 $\alpha$  (IL-1 $\alpha$ ), interleukin-1 $\beta$  (IL-1 $\beta$ ), interleukin 6 (IL-  
3 6), and tumor necrosis factor (TNF- $\alpha$ ).
- 1 15. The method of claim 13, wherein the anti-inflammatory mediator is selected from  
2 the group consisting of interleukin 1 receptor antagonist (IL-1RA), tumor necrosis factor  
3 receptor antagonist (TNF-RA) or derivatives thereof, soluble TNF receptors, anti-TNF  
4 antibodies, and anti-TNF-RA antibodies.
- 1 16. The method of claim 1, further comprising the step of administering one or more  
2 cytokines, chemokines, interferons or hormones to the tissue, body fluid or cell.
- 1 17. The method of claim 16, wherein the chemokine is selected from the group  
2 consisting of interleukin-8 (IL-8).
- 1 18. The method of claim 16, wherein the peptide hormone is selected from the group  
2 consisting of vasoactive intestinal peptide (VIP).

- 1 19. The method of claim 1, wherein the tissue comprises blood.
- 1 20. The method of claim 1, wherein the tissue comprises nucleated cells.
- 2 21. The method of claim 1, wherein the cell is selected from the group consisting of a  
3 monocyte, a macrophage, a neutrophil, a T-cell, a B-cell, a basophil, a fibroblast, an  
4 endothelial cell and an epithelial cell.
- 1 22. The method of claim 1, wherein the tissue comprises buccal cells.
- 1 23. The method of claim 1, wherein the tissue comprises a biopsy sample.
- 1 24. The method of claim 1, wherein the tissue sample is stored in a stabilization  
2 solution prior to analysis.
- 1 25. The method of claim 1, wherein the tissue sample is stored frozen.
- 1 26. The method of claim 1, wherein the first gene encodes serum amyloid A1 (*SAA1*).
- 1 27. The method of claim 1, wherein the second gene encodes serum amyloid A2  
2 (*SAA2*).
- 1 28. The method of claim 1, wherein the first gene or second gene encodes a  
2 chemokine, a cytokine agonist, a cytokine antagonist, or a complement component.
- 1 29. The method of claim 1, further comprising the step of quantifying the RNA level  
2 of a third gene and comparing the RNA level from the third gene to the RNA level from  
3 the first gene and the RNA level from the second gene.
- 1 30. The method of claim 29, wherein the third gene encodes an acute phase reactant.
- 1 31. The method of claim 29, wherein the third gene encodes a chemokines, cytokine  
2 agonist, a cytokine antagonist, or a complement component.

- 1 32. The method of claim 29, wherein the third gene is selected from the group  
2 consisting of C-reactive Protein (*CRP*), complement component 3 (*C3*), Factor B, and  
3 albumin.
- 1 33. The method of claim 1, wherein the subject suffers from an inflammatory  
2 condition, a disease with an inflammatory component, a disease with an inflammatory  
3 consequence, and/or a disease with inflammatory symptoms.
- 1 34. The method of claim 1, wherein the subject is being evaluated as a candidate for,  
2 is about to undergo, or has undergone a tissue or organ transplant.
- 1 35. The method of claim 1, wherein the subject may be refractory, less responsive, or  
2 more responsive to steroid treatment.
- 1 36. The method of claim 1, wherein the subject has cancer, is being treated for cancer,  
2 or is in remission for cancer.
- 1 37. The method of claim 1, wherein the cancer is selected from the group consisting  
2 of solid tumors, acute lymphocytic leukemia and lymphoma.
- 1 38. The method of claim 1, wherein the subject is steroid dependent.
- 1 39. The method of claim 1, wherein the subject suffers from an arthritic disease.
- 1 40. The method of claim 39, wherein the arthritic disease is osteoarthritis, rheumatoid  
2 arthritis, thoracic arthritis or idiopathic arthritis.
- 1 41. The method of claim 1, wherein the subject suffers from an autoimmune disease.
- 1 42. The method of claim 1, wherein the subject suffers from an inflammatory bowel  
2 disease.
- 1 43. The method of claim 42, wherein the subject suffers from Crohn's disease or  
2 ulcerative colitis.

1 44. The method of claim 1, wherein the subject suffers from asthma, adult respiratory  
2 distress syndrome, systemic lupus erythematosus, inflammatory bowel disease, Crohn's  
3 disease, ulcerative colitis, multiple sclerosis, insulin-dependent diabetes mellitus,  
4 autoimmune arthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic  
5 arthritis, inflammatory pulmonary syndrome, pemphigus vulgaris, idiopathic  
6 thrombocytopenic purpura, cerebral edema, autoimmune meningitis, myasthenia gravis,  
7 autoimmune thyroiditis, sarcoidosis, dermatitis, atopic dermatitis, eczematous dermatitis,  
8 psoriasis, Sjogren's Syndrome, sarcoidosis, keratoconjunctivitis sicca secondary to  
9 Sjogren's Syndrome, alopecia areata, allergic responses due to arthropod bite reactions,  
10 aphthous ulcer, iritis, conjunctivitis, keratoconjunctivitis, cutaneous lupus erythematosus,  
11 scleroderma, vaginitis, proctitis, drug eruptions, Stevens-Johnson syndrome, leprosy  
12 reversal reactions, erythema nodosum leprosum, autoimmune uveitis, allergic  
13 encephalomyelitis, aplastic anemia, pure red cell anemia, autoimmune destruction of  
14 erythrocytes, idiopathic thrombocytopenia, polychondritis, Wegener's granulomatosis,  
15 chronic active hepatitis, alcohol liver disease, Graves ophthalmopathy, primary biliary  
16 cirrhosis, uveitis posterior and interstitial lung fibrosis or a combination thereof.

1 45. The method of claim 1, wherein the subject suffers from a renal , allergic,  
2 infectious, ocular, skin, gastrointestinal, and/or endocrine disease.

1 46. The method of claim 1, wherein the subject suffers from stroke, coronary artery  
2 disease, vascular disease, atherothrombotic disease and/or spinal cord injury.

1 47. The method of claim 1, wherein the subject suffers from an endocrine disease.

1 48. The method of claim 1, wherein the subject is being evaluated as a candidate for,  
2 is about to undergo, or has undergone steroid replacement or substitution therapy.

1 49. The method of claim 1, wherein the subject suffers from acute adrenal  
2 insufficiency, chronic primary adrenal insufficiency, secondary adrenal insufficiency,  
3 and/or congenital adrenal hyperplasia.



1 50. The method of claim 1, wherein the first gene is controlled by a steroid responsive  
2 element.

1 51. The method of claim 50, wherein the steroid responsive element is a  
2 glucocorticoid responsive element (GRE).

1 52. The method of claim 51, wherein the GRE is a consensus GRE or a non-  
2 consensus GRE.

1 53. The method of claim 52, wherein the consensus GRE is GGTACAnnnTGTTCT  
2 or a variation thereof, where n is any nucleotide.

1 54. The method of claim 1, wherein the second gene is encoded by a gene which is  
2 not controlled by a steroid response element.

1 55. The method of claim 1, wherein the steroid is a glucocorticoid, an estrogen, or an  
2 androgen.

1 56. The method of claim 1, further comprising the step of administering one or more  
2 glucocorticoid inhibitors, glucocorticoid antagonists or other steroid inhibitors or steroid  
3 antagonists.

1 57. The method of claim 56, wherein the glucocorticoid inhibitor is selected from the  
2 group consisting of mitotane, metyrapone, aminoglutethimide, ketoconazole, and  
3 trilostane.

1 58. The method of claim 1, wherein the steroid is selected from the group consisting  
2 of alclometasone dipropionate, amcinonide, beclomethasone dipropionate,  
3 betamethasone, betamethasone benzoate, betamethasone dipropionate, betamethasone  
4 sodium phosphate, betamethasone sodium phosphate and acetate, betamethasone  
5 valerate, clobetasol propionate, clocortolone pivalate, cortisol (hydrocortisone), cortisol  
6 (hydrocortisone) acetate, cortisol (hydrocortisone) butyrate, cortisol (hydrocortisone)  
7 cypionate, cortisol (hydrocortisone) sodium phosphate, cortisol (hydrocortisone) sodium  
8 succinate, cortisol (hydrocortisone) valerate, cortisone acetate, desonide, desoximetasone,

9 dexamethasone, dexamethasone acetate, dexamethasone sodium phosphate, diflorasone  
10 diacetate, fludrocortisone acetate, flunisolide, fluocinolone acetonide, fluocinonide,  
11 fluorometholone, flurandrenolide, halcinonide, medrysone, methylprednisolone,  
12 methylprednisolone acetate, methylprednisolone sodium succinate, mometasone furoate,  
13 paramethasone acetate, prednisolone, prednisolone acetate, prednisolone sodium  
14 phosphate, prednisolone tebutate, prednisone, triamcinolone, triamcinolone acetonide,  
15 triamcinolone diacetate, triamcinolone hexacetonide or a synthetic analog thereof, or a  
16 combination thereof.

1 59. The method of claim 1, wherein the steroid is administered parenterally, orally or  
2 locally.

1 60. The method of claim 1, wherein the steroid is administered intravenously,  
2 intramuscularly, enterally, transdermally, nasally, transmucosally, via inhalation, and/or  
3 subcutaneously.

1 61. A kit for determining steroid responsiveness in a subject comprising:  
2 primers specific for amplifying RNA encoded by a first gene that is responsive to  
3 steroid; and  
4 primers specific for amplifying RNA encoded by a second gene that is not  
5 responsive the steroid.

1 62. The kit of claim 61, further comprising a tissue, body fluid or cell collector.